This Page Is Inserted by IFW Operations and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents will not correct images, please do not report the images to the Image Problem Mailbox.

WHAT IS CLAIMED IS:

A compound of having the following formula: 1.

$$A-(CH_2)_{\overline{m}}X-(CH_2)_{\overline{n}}D$$
 X
 R^{11}
 R^{11}

wherein:

5

10

15

A is a member selected from the group consisting of: R², -NR³R⁴,

ŅR⁶

 $-C(=O)NR^3R^4$,

R⁵

where R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are independently selected from the group consisting of H, -OH, C_{1.8}alkyl, C_{2.8}alkenyl, C_{2.8}alkynyl, C_{3.8}cycloa kyl,

C₆₋₁₂carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and

C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where R⁶ taken with either of R⁷ and R⁸, and/or R⁷ taken with R⁸, can each form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of

m is an integer from 0-3;

Z is a member selected from the group consisting of a direct link, $C_{1.8}$ alkyl, C₃₋₈cycloalkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₁₋₈carbocyclic aryl, or a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, Q and S;

n is an integer from 0-3;

D is a member selected from the group consisting of a direct link, -CH₂-, -O-, $-N(R^2)$ -, -C(=O)-, -S-, $-SO_2$ -, $-SO_2$ -, $-N(R^2)$ -, $-N(R^2)$ - SO_2 -, -OC(=O)-, -C(=O)O-, 10 $-C(=O)-N(R^2)$ - and $-N(R^2)-C(=O)$;

R¹ is a member selected from the group consisting of H, C_{1.8}alkyl, C_{2.8}alkenyl, C_{2.8}alkynyl, C_{3.8}cycloalkyl, halogen, polyhaloalkyl, C_{0.8}alkyl-C(=O)OH, $C_{0.8}$ alkyl- $C(=O)O-C_{1.8}$ alkyl, -CN, -NO₂, $C_{0.8}$ alkyl-OH, $C_{0.8}$ alkyl-SH, -C(=O)NR²R³, -O-R² and -O-C(=O)R², an unsubstituted aming group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1.8}alkyl, C_{2.8}alkenyl, C₂. ₈alkynyl, C₃₋₈cycloalkyl, polyhaloalkyl, -SO₂R², C₀₋₈alkyl-C(=O)OH and C_{0.8}alkyl-C(=0)O-C_{1.8}alkyl, where R² and R³ is as described above;

20

15

q is an integer from 0-3;

X is N or $-CR^{12}$;

R¹¹ and R¹² are independently a member selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, $C_{1\text{--}6}alkylaryl,\ C_{1\text{--}6}alkyl-C_{3\text{--}8}cycloalkyl,\ -O-R^2,\ -O-C(=O)R^2,\ -C_{1\text{--}8}alkyl-O-R^{10},$ $-C_{1.8}$ alkyl-O-C(=O)R¹⁰, $-C_{1.8}$ alkyl-C(=O)OR¹⁰, $-C_{1.8}$ alkyl-O-C(=O)OR¹⁰, $-C_{1.8}$ alkyl- $C(=O)NR^{10}R^{10}$, $-C_{1.8}$ alkyl- $NR^{10}R^{10}$, $-C_{1.8}$ alkyl- $NR^{10}C(=O)R^{10}$, $-SR^{10}$, where R^2 is as described above and R^{10} is a member selected from the group consisting of N,

15

20

25

C_{1.8}alkyl, C_{2.8}alkenyl, C_{2.8}alkynyl, and wherein when two R¹⁰ groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

p is an integer from 0-3;

E is a member selected from the group consisting of a direct link, -O-, -N(-R¹¹)-, where R¹¹ is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group containing 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to R^{14} groups;

J is a member selected from the group consisting of a direct link, a bivalent C_{3-8} cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group containing 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

each R^{14} group is a member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, halogen, polyhaloalkyl, $C_{0.8}$ alkyl-C(=O)OH, $C_{0.8}$ alkyl- $C(=O)O-C_{1.8}$ alkyl, -CN, -NO₂, $C_{0.8}$ alkyl-OH, $C_{0.8}$ alkyl-SH, -O- R^2 and -O- $C(=O)R^2$, an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, polyhaloalkyl, $C_{0.8}$ alkyl-C(=O)OH and $C_{0.8}$ alkyl- $C(=O)O-C_{1.8}$ alkyl;

DOYFERFUL DECIS

G is a member selected from the group consisting of: H; -CN; -OR¹⁷;

wherein

5

10

15

t is an integer from 0 to 6,

u is the integer 0 or 1, and R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵ and R²⁶ are independently selected from the group consisting of H, OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where r¹⁸ taken with R¹⁹, R²² taken with either of R²⁴ and R²⁵, and R²¹ taken with R²⁵, can each independently form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, -CN, -OR¹⁷, either E or J must contain at least one N atom;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.



A compound of formula II:

A-Z-D
$$\mathbb{R}^{11}$$

$$(\mathbb{R}^{1})_{q}$$

$$(\mathbb{C}H_{2})_{p}$$
 \mathbb{E}
 $\mathbb{C}J$

A is a member selected from the group consisting of: R², -NR³R⁴,

5 $-C(=O)NR^3R^4$,

$$\begin{array}{c}
NR^{6} \\
NR^{7}R^{8};\\
R^{5}
\end{array}$$

$$\begin{array}{c}
NR^{6} \\
NR^{7}R^{8};\\
NR^{6} \\
R^{9}
\end{array}$$
and
$$\begin{array}{c}
NR^{6} \\
R^{9}
\end{array}$$

where R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are independently selected from the group consisting of H, -OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S, and C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where r⁶ taken with either of R⁷ and R⁸, and/or R⁷ taken with R⁸, can each form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of N, O and S;

Z is a member selected from the group consisting of a direct link, C_{1.8}alkyl,

C₃₋₈cycloalkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₁₋₈carbocyclic aryl, or a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S;

ant :

D is a member selected from the group consisting of a direct link, -CH₂-, -O-, -N(R²)-, -C(\neq O)-, -S-, -SO₂-, -SO₂-N(R²)-, -N(R²)-SO₂-, -OC(=O)-, -C(=O)-N(R²)-and -N(R²)-C(=O)-;

R¹ is a member selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, halogen, polyhaloalkyl, C₀₋₈alkyl-C(=O)OH, C₀₋₈alkyl-C(=O)O-C₁₋₈alkyl, -CN, -NO₂, C₀₋₈alkyl-OH, C₀₋₈alkyl-SH, -C(=O)NR²R³, -O-R² and -O-C(=O)R², an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, polyhaloalkyl, -SO₂R², C₀₋₈alkyl-C(=O)OH and C₀₋₈alkyl-C(=O)O-C₁₋₈alkyl, where R² and R³ is as described above;

15

10

q is an integer from 0-3;

R¹¹ is independently a member selected from the group consisting of H,

C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, C₁₋₆alkylaryl,

C₁₋₆alkyl-C₃₋₈cycloalkyl, -O-R², -O-C(=O)R², -C₁₋₈alkyl-O-R¹⁰, -C₁₋₈alkyl-O-C(=O)R¹⁰,

-C₁₋₈alkyl-C(=O)OR¹⁰, -C₁₋₈alkyl-O-C(=O)OR¹⁰, -C₁₋₈alkyl-C(=O)NR¹⁰R¹⁰,

-C₁₋₈alkyl-NR¹⁰R¹⁰, -C₁₋₈alkyl-NR¹⁰C(=O)R¹⁰, -SR¹⁰, where R² is as described above and R¹⁰ is a member selected from the group consisting of H, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, and wherein when two R¹⁰ groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

25

p is an integer from 0-2;

E is a member selected from the group consisting of a direct link, -0-, -N(-R¹¹)-, where R¹¹ is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group containing 1 to 4 heteroatoms selected from the group consisting of

15

N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R^{14} groups;

J is a member selected from the group consisting of a direct link, a bivalent C₃₋₈cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group containing 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R¹⁴ groups;

each R^{14} group is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, halogen, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH, C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl, -CN, -NO₂, C_{0-8} alkyl-OH, C_{0-8} alkyl-SH, -O- R^2 and -O-C(=O) R^2 , an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH and C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl;

G is a member selected from the group consisting of: H; -CN; -OR¹⁷;

$$(CH_2)$$
 (CH_2)
 $($

15

20

wherein

t is an integer from 0 to 6,

u is the integer 0 or 1, and R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵ and R²⁶ are independently selected from the group consisting of H, -OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where r¹⁸ taken with R¹⁹, R²² taken with either of R²⁴ and R²⁵, and R²⁴ taken with R²⁵, can each independently form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, CN, -OR¹⁷, either E or J must contain at least one N atom;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

- 3. A compound of claim 2, wherein D is a member selected from the group consisting of: -O-, -N- \mathbb{R}^2 , -C(=O)-, -S-, -SO₂-, -SO₂-NR², -NR²-SO₂, -OC(=O)-, -C(=O)NR², and -NR²-C(=O)-.
- 4. A compound of claim 3, wherein D is a member selected from the group consisting of: -O-, -NR², -C(=O)₅, -S-, and -SO₅.

5. A compound of formula III:

pul as

$$\begin{array}{c|c}
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & & & \\
 & &$$

5 wherein:

10

15

20

 R^8 is selected from the group consisting of H, -OH, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1-6} alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

 R^1 is a member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, halogen, polyhaloalkyl, $C_{0.8}$ alkyl-C(=O)OH, $C_{0.8}$ alkyl-C(=O)O- $C_{1.8}$ alkyl, -CN, -NO₂, $C_{0.8}$ alkyl-OH, $C_{0.8}$ alkyl-SH, -C(=O)NR²R³, -O-R² and -O-C(=O)R², an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, polyhaloalkyl, -SO₂R², $C_{0.8}$ alkyl-C(=O)OH and $C_{0.8}$ alkyl-C(=O)O- $C_{1.8}$ alkyl, where R² and R³ is as described above;

R² is selected from the group consisting of H, -OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

25 q is 0-3;

10

15

 R^{11} is a member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, $C_{6.12}$ carbocyclic aryl, $C_{1.6}$ alkylaryl, $C_{1.6}$ alkyl- $C_{3.8}$ cycloalkyl, $-O-R^2$, $-O-C(=O)R^2$, $-C_{1.8}$ alkyl- $-O-R^{10}$, $-C_{1.8}$ alkyl- $-O-C(=O)R^{10}$, $-C_{1.8}$ alkyl- $-O-C_{1.8}$ alkyl--

p is an integer from 0.2;

E is a member selected from the group consisting of a direct link, -O-, -N(-R¹¹)-, where R¹¹ is as set forth above, phenylene, a bivalent 5 to 12 member heteroaryl group containing 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S, wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R¹⁴ groups;

J is a member selected from the group consisting of a direct link, a bivalent C₃₋₈cycloalkyl group, phenylene, a 5 to 12 member bivalent heteroaryl group containing 1 to 4 heteroatoms selected from the group consisting of N, O and S, and a five to ten membered non-aromatic bivalent heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S wherein said heteroaryl and said non-aromatic heterocyclic ring structure may be independently substituted by from 0 to 5 R¹⁴ groups;

each R^{14} group is a member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, halogen, polyhaloalkyl, $C_{0.8}$ alkyl- $C(=O)O+C_{1.8}$ alkyl, -CN, - NO_2 , $C_{0.8}$ alkyl- $O+C_{0.8}$ alkyl- $C+C_{0.8}$ alkyl- $C+C+C_{0.8}$ alkyl- $C+C+C+C_{0.8}$ alkyl- $C+C+C+C_{0.8}$ alkyl- $C+C+C+C_{0.8}$ alkyl-C+C+C+C+Calkyl-C+C+C+Calkyl-C+C+C+CAlkyl-C+C

25

20

C_{3.8}cycloalkyl, polyhaloalkyl, C_{0.8}alkyl-C(=O)OH and C_{0.8}alkyl-C(=O)O-C_{1.8}alkyl;

G is a member selected from the group consisting of: H; -CN; -OR¹⁷;

wherein

t is an integer from 0 to 6,

5

10

15

u is the integer 0 or 1, and R^{17} , R^{18} , R^{19} , R^{20} , R^{21} , R^{22} , R^{23} , R^{24} , R^{25} and R^{26} are independently selected from the group consisting of H, -OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂. salkynyl, C3.scycloalkyl, C6.12 carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1.6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where r¹⁸ taken with R¹⁹, R²² taken with either of R²⁴ and R²⁵, and R²⁴ taken with R²⁵, can each independently form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, -CN, -OR¹⁷, either E or J must contain at least one N atom;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

- 6. A compound of claim 5, wherein R^1 and R^8 are independently a lower alkyl group and R^{11} is hydrogen or is a C_1 to C_8 alkyl group.
- 7. A compound of claim 5, wherein q is zero and R⁸ is lower alkyl group.
- 8. A compound of claim 5, wherein:
- 5 R⁸ is a methyl group;

p is an integer from 1-2;

E is selected from the group consisting of: a direct link,

$$\stackrel{\text{S}}{\searrow}_{N}$$
, $\stackrel{\text{N}}{\searrow}_{N-}$, $\stackrel{\text{N}}{\longrightarrow}_{N-}$, $\stackrel{\text{N}}{\searrow}_{N-}$, $\stackrel{\text{N}}{\Longrightarrow}_{N-}$, $\stackrel{\text{N}}{\Longrightarrow}_{$

J is selected from the group consisting of:

and G is selected from the group consisting of:



9. A compound of formula IV:

$$A-Z-(CH_2)_{\Pi}-D$$
 N
 O
 R^{11}
 G
 $(R^{14})_{0-3}$
 (IV)

wherein:

A is a member selected from the group consisting of: R^2 , $-NR^3R^4$, $-C(=O)NR^3R^4$,

$$\begin{array}{c}
NR^6 \\
NR^7R^8 \\
R^5
\end{array}$$

$$\begin{array}{c}
NR^6 \\
NR^7R^8 \\
\end{array}$$

$$\begin{array}{c}
NR^6 \\
R^9 \\
\end{array}$$
and

where R², R³, R⁴, R⁵, R⁶, R⁷, R⁸, and R⁹ are independently selected from the group consisting of H, -OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl,

a3 cont

10

20

30

C_{0,12}carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C₁₋₆alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where r⁶ taken with either of R⁷ and R⁸, and/or R⁷ taken with R⁸, can each form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of N, O and S;

Z is a member selected from the group consisting of a direct link, C₁₋₈alkyl, C₃₋₈cycloalkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₁₋₈carbocyclic aryl, or a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S;

n is 0-3;

D is a member selected from the group consisting of: $-CH_2$ -, -O-, $-N R^2$, -C(=O)-, -S-, $-SO_2$ -, $-SO_2$ -, $-NR^2$ -, $-NR^2$ -SO₂, -OC(=O)-, $-C(=O)NR^2$, and $-NR^2$ -C(=O)-;

 R^1 and R^{14} are independently a member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, halogen, polyhaloalkyl, $C_{0.8}$ alkyl-C(=O)OH, $C_{0.8}$ alkyl-C(=O)O-C_{1.8}alkyl, -CN, NO₂, $C_{0.8}$ alkyl-OH, $C_{0.8}$ alkyl-SH, -O- R^2 and -O-C(=O) R^2 , an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, $C_{3.8}$ cycloalkyl, polyhaloalkyl, $C_{0.8}$ alkyl-C(=O)OH and $C_{0.8}$ alkyl-C(=O)O- $C_{1.8}$ alkyl;

25 q is 0-3;

 $R^{11} \text{ is a member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, C_{6-12} carbocyclic aryl, C_{1-6} alkyl-O-R$^{10}, $-C_{1-8}$ alkyl-O-C(=O)R$^{10}, $-C_{1-8}$ alkyl-O-C(=O)NR$^{10}, $-C_{1-8}$ alkyl-C(=O)NR$^{10}, $-C_{1-8}$ alkyl-C(=O)NR$^{10}, $-C_{1-8}$ alkyl-O-C(=O)NR$^{10}, $-C_{1-8}$ alkyl-$

 $C_{1.8}$ alkyl-NR¹⁰R¹⁰, $-C_{1.8}$ alkyl-NR¹⁰C(=O)R¹⁰, $-SR^{10}$, where R² is as described above and R¹⁰ is a member selected from the group consisting of H, $C_{1.8}$ alkyl, $C_{2.8}$ alkenyl, $C_{2.8}$ alkynyl, and wherein when two R¹⁰ groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

G is a member selected from the group consisting of: H; -CN; -OR¹⁷;

$$(CH_{2}) \xrightarrow{\text{NR}^{23}} \text{NR}^{24} \text{R}^{25} ;$$

$$NR^{23} \xrightarrow{\text{NR}^{24}} \text{R}^{25} ;$$

wherein

10

15

t is an integer from 0 to 6,

u is the integer 0 or 1, and R¹⁷, R¹⁸, R¹⁹, R²⁰, R²¹, R²², R²³, R²⁴, R²⁵ and R²⁶ are independently selected from the group consisting of H, OH, C_{1.8}alkyl, C_{2.8}alkenyl, C_{2.8}alkynyl, C_{3.8}cycloalkyl, C_{6.12}carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C_{1.6}alkylheterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S; where r¹⁸ taken with R¹⁹, R²² taken with either of R²⁴ and R²⁵, and R²⁴ taken with R²⁵, can each independently form a 5 to 6 membered heterocyclic ring containing from 1 to 4 atoms selected from the group consisting of N, O and S;

with the proviso that when G is H, -CN, -OR¹⁷, either E or J must contain at least one N atom;

ant cont

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

10. A compound of claim 9, wherein R¹, R⁸, R¹¹ and R¹⁴ are independently selected from the group consisting of hydrogen, methyl and ethyl;

A is selected from the group consisting of: -H, -CH₃, -NH₂, -C(O)N(CH₃)₂,

$$H_3C$$
 $\stackrel{NH}{\longrightarrow}$, H_2N $\stackrel{NH}{\longrightarrow}$, NH , NH , NH , NH , NH , NH , and NH ;

Z is selected from the group consisting of:

10

n is an integer from 0-2; and

D is selected from the group consisting of: -O-, -N(CH₃)-, and -CH₂-.



A compound of formula V: 11.

wherein:

R², R⁶, and R⁹ are independently selected from the group consisting of H, -OH, C₁₋₈alkyl, C₂₋₈alkenyl, C₂₋₈alkynyl, C₃₋₈cycloalkyl, C₆₋₁₂carbocyclic aryl, a five to ten membered heterocyclic ring system containing 1-4 heteroatoms selected from the group consisting of N, O and S; and C₁₋₆alky theterocyclic ring system having in the ring system 5 to 10 atoms with 1 to 4 of such atoms being selected from the group consisting of N, O and S;

10

15

5

R¹¹ is independently a member selected from the group consisting of H, C_{1.8}alkyl, C_{2.8}alkenyl, C_{2.8}alkynyl, C_{3.8}cycloalkyl, C_{6.12}carbocyclic aryl, C_{1.6}alkylaryl, $C_{1.6}$ alkyl- $C_{3.8}$ cycloalkyl, -O- R^2 , -O-C(=O) R^2 , - $C_{1.8}$ alkyl-Q- R^{10} , - $C_{1.8}$ alkyl-O-C(=O) R^{10} , $-C_{1.8}$ alkyl- $C(=O)OR^{10}$, $-C_{1.8}$ alkyl- $O-C(=O)OR^{10}$, $-C_{1.8}$ alkyl- $C(=O)NR^{10}R^{10}$, $-C_{1.8}$ alkyl-NR¹⁰R¹⁰, $-C_{1.8}$ alkyl-NR¹⁰C(=O)R¹⁰, $-SR^{10}$, where R is as described above and R¹⁰ is a member selected from the group consisting of H, $\mathcal{C}_{1.8}$ alkyl, C_{2.8}alkenyl, C₂. salkynyl, and wherein when two R¹⁰ groups are present they may be taken together to form a saturated or unsaturated ring with the atom to which they are both attached;

20

each R¹⁴ group is a member selected from the group consisting of H, C_{1.8}alkyl, C₂. $_{8}$ alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, halogen, polyhaloalkyl, C_{0-8} alkyl- \dot{C} (=O)OH, $C_{0.8}$ alkyl- $C(=O)O-C_{1.8}$ alkyl, -CN, -NO₂, $C_{0.8}$ alkyl-OH, $C_{0.8}$ alkyl-SH, -O-R and -O-C(=O)R², an unsubstituted amino group, a mono- or di-substituted amino group, wherein the substituted amino groups are independently substituted by at least one

QY conf

member selected from the group consisting of H, C_{1-8} alkyl, C_{2-8} alkenyl, C_{2-8} alkynyl, C_{3-8} cycloalkyl, polyhaloalkyl, C_{0-8} alkyl-C(=O)OH and C_{0-8} alkyl-C(=O)O- C_{1-8} alkyl;

and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

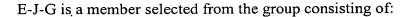
12. A compound having the following structure:

10

wherein:

A-Z is a member selected from the group consisting of:

15



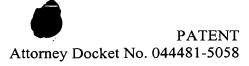
and all pharmaceutically acceptable isomers, salts, hydrates, solvates and prodrug derivatives thereof.

- 13. A pharmaceutical composition for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound as in one of claims 1-12.
- 14. A method for preventing or treating a condition in a mammal characterized by undesired thrombosis comprising administering to said mammal a therapeutically effective amount of a compound as in one of claims 1-12.
- 15. The method of claim 14, wherein the condition is selected from the group consisting of:

acute coronary syndrome, myocardial infarction, unstable angina, refractory angina, occlusive coronary thrombus occurring post-thrombolytic therapy or post-

5





coronary angioplasty, a thrombotically mediated cerebrovascular syndrome, embolic stroke, thrombotic stroke, transient ischemic attacks, venous thrombosis, deep venous thrombosis, pulmonary embolus, coagulopathy, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, thromboangiitis obliterans, thrombotic disease associated with heparin-induced thrombocytopenia, thrombotic complications associated with extracorporeal circulation, thrombotic complications associated with instrumentation such as cardiac or other intravascular catheterization, intra-aortic balloon pump, coronary stent or cardiac valve, and conditions requiring the fitting of prosthetic devices.

10

5

16. A method for inhibiting the coagulation of biological samples comprising the administration of a compound as in one of claims 1-12.